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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,087	09/29/2003	Jianzhu Chen	0492611-0507 (MIT 10396)	2178
24280 7590 03/11/2008 CHOATE, HALL & STEWART LLP TWO INTERNATIONAL PLACE BOSTON, MA 02110			EXAMINER CHONG, KIMBERLY	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/674,087	Applicant(s) CHEN ET AL.	
	Examiner Kimberly Chong	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 December 2006 and 08 February 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38-49, 81-90 and 98-100 is/are pending in the application.
- 4a) Of the above claim(s) 43-48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-42, 49, 81-90 and 98-100 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/18/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/08/2007 has been entered.

Status of Application/Amendment/Claims

Applicant's response filed 12/14/2006 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 07/12/2006 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 38-49, 81-90 and 98-100 are pending. Claims 38-42, 49, 81-90 and 98-100 are under examination and claims 43-48 and the non-elected subject matter are withdrawn as being drawn to a non-elected invention.

Information Disclosure Statement

The information disclosure statement filed on 12/18/2006 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because of the following reasons:

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The non-patent literature documents Tompkins et al., Verma et al. and Zhang et al. have not been considered because they have not been made of record. It appears the documents were damaged and were not able to be scanned into the file. Applicant must resubmit the above noted documents in order for them to be considered by the Examiner. Also it must be noted that only the English abstract and the English claims of foreign document EP1144623 have been considered. Signed copies indicating the considered references have been placed in the file.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 38-42, 49, 81-90 and 98-100 are provisionally rejected under the judicially created doctrine of double patenting over claims 12, 22 and 24-27 of copending

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Application No. 11/259,434. This is a provisional double patenting rejection since the conflicting claims have not yet been patented. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of the patent are drawn to patently indistinguishable subject matter.

The claims are drawn to methods of inhibiting a transcript associated with a influenza virus, or methods of treating or preventing or treating an influenza virus or a clinical condition associated with overexpression or inappropriate expression of an influenza transcript, comprising administering an siRNA in combination with a cationic polymer, wherein said administration may be intravenous or intranasal, or is inhaled, or is delivered by aerosol, or wherein said inhibition is in the lung, or not in the lung, or wherein said combination is delivered with a delivery enhancing agent which may be an antibody or fragment or ligand.

Claims 12, 22 and 24-27 of co-pending Application No. 11/259,434 are drawn to a method of treating influenza virus infection comprising contacting the host cells with an antiviral compound comprising an antisense oligonucleotide wherein the oligonucleotide is conjugated to a polypeptide that enhances uptake of the compound into the host cell. Co-pending Application No. 11/259,434 does not teach inhibiting expression of influenza virus or treating influenza virus using a siRNA and do not teach using a delivery agent such as a cationic polymer. Tuschl et al. (WO 02/44321) teach the use of siRNA compounds to inhibit gene expression. Tuschl et al. teach siRNA are the new alternative to antisense compounds and have improved efficacy and safety (see page 3). Gautam et al. (Molecular Therapy 2000, Vol. 2(1); 63-70) teach a method

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of efficiently delivery nucleic acids along with a cationic polymer, polyethyleneimine, into the lungs of a mouse (see Figure 1). It would have been obvious and one of skill in the art would have been motivated to use an siRNA in a method of treating influenza virus given Tuschl et al. teach siRNAs are the new alternative to antisense therapeutics.

Further, it would have been obvious and one of skill in the art would have been motivated to deliver the siRNA using a cationic polymer PEI given Gautam et al. teach efficient delivery of nucleic acids into cells using PEI.

Thus claims 12, 22 and 24-27 of co-pending Application No. 11/259,434 anticipates claims 38-42, 49, 81-90 and 98-100 of the instant application. This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-42, 49, 84-90 and 99 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventor(s) at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to methods of inhibiting any transcript associated with influenza virus, or methods of treating or preventing influenza virus or a clinical condition associated with overexpression or inappropriate expression of an influenza virus transcript, comprising administering an siRNA in combination with a cationic polymer. It is noted that claims 81-83, 99 and 100, drawn to inhibition of a target transcript of a respiratory virus in a mammalian subject, is considered to have adequate description, because although the claims are broadly drawn to inhibiting any sequence of any respiratory virus or influenza virus, such inhibition is not claimed as having the function of being linked to treating or preventing any disease. It is the lack of nexus linking such a broad genera of structures (any siRNA targeted to any influenza virus or any transcript associated with influenza virus) with such a specific function of treating or preventing influenza virus that necessitates this rejection.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Thus, an applicant complies with the written-description requirement by describing the invention, with all its claimed limitations, and by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical, structure/function correlation,

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methods of making the claimed product, and any combination thereof. The representative sample requirement may be satisfied by supplying structural or functional information, or a combination of both, such that one of skill in the art would be satisfied that applicants were in possession of the genus as claimed. Further, the size of the representative sample required is an inverse function of the unpredictability of the art.

At the outset it is noted that the rejected claims do not recite any sequence identifier relating to an influenza virus or any transcript associated with influenza virus. Nor do the claims identify by name any particular influenza virus or any transcript associated with influenza virus. At their most specific, the claims merely recite methods of inhibiting any transcript associated with an influenza virus using and siRNA/cationic complex. It is further claimed that via the use of such complexes in the instant methods, any condition associated with influenza virus will be prevented.

In contrast, the specification exemplifies only the use of siRNA oligos complexed with PEI in methods of inhibiting specific elements of the influenza genome in vivo. While the instant specification is considered to provide adequate description for methods of inhibiting influenza virus using such siRNA/cationic complexes, this is not considered to be representative of the breadth claimed, since at their narrowest, the claims are very broadly drawn to methods of inhibiting any transcript associated with any influenza virus. Accordingly these claims embrace, at their minimum, siRNA directed to any sequence of any gene expression any transcript associated with influenza virus, known or yet to be discovered, along with any isoform or allele present within any influenza viral species, or any variant, polymorphic or otherwise, that is within

reasonable similarity to these viral families that retain infectivity, such that disease treatment or prevention is achieved. The instant specification is not considered to have described such breadth of structure linked to such breadth of function.

The specification does not provide specific guidance that would allow the skilled artisan to recognize that Applicant was in possession of the instant invention, commensurate in scope with what is now claimed.

Thus, the instantly claimed invention cannot be said to have been adequately described in a way that would convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the claimed invention.

Claims 49, 84-90 and 99 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting and treating influenza virus by reducing viral titer in chicken embryos administered siRNA targeted to a viral polymerase and nucleoprotein, does not reasonably provide enablement for a method of *prevention* of influenza virus or a *prevention* of a clinical condition associated with overexpression or inappropriate expression of an influenza virus transcript. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The instant claims are drawn to a method for the *prevention* of influenza virus or a *prevention* of a clinical condition associated with overexpression or inappropriate expression of an influenza virus transcript. The specification as filed discloses inhibition

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of a viral RNA polymerase and nucleoprotein using a siRNA and disclose inhibition of expression of these transcripts inhibit influenza A virus product in chicken embryos.

The specification as filed does not teach that because of administration of a siRNA compound targeted to any transcript of influenza virus or any transcript associated with influenza virus, prevention of influenza virus is provided in a patient.

There is no guidance in the specification as filed that teaches how to prevent influenza virus by targeting the claimed siRNA compound to human cells or tissues and inhibiting the expression influenza virus or inhibit the expression of any transcript associated with influenza virus. Although the specification discloses the relationship of decreased expression of Viral RNA polymerase and nucleoprotein, such a disclosure would not be considered enabling since the state of therapeutic siRNA-mediated gene inhibition for prevention of disease is highly unpredictable.

The following factors have been considered in the analysis of enablement: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claimed breadth of claims 49, 84-89 and 99 encompass methods of preventing influenza virus or any transcript associated in influenza virus by use of siRNA in vivo. Although the specification teaches Influenza A virus can be inhibited using siRNA targeted to viral polymerase and nucleoprotein, this guidance is not

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sufficient to resolve the known unpredictability in the art associated with prevention of viral diseases, particularly influenza virus using an siRNA.

The post-filing references cited herein illustrate the state of the art for therapeutic *in vivo* applications using siRNA compounds to prevent viral infections: Lecellier et al. (Immunological Reviews 2004, Vol. 195: 285-303) notes a major problem with RNAi-based antiviral approaches is the fact that "...the abundance of viral targets could out-titer the degradation machinery of RNA silencing, especially if the RNAi effect is only transient. Moreover, once initiated in the cell, active replication could take place in specific subcellular compartments that may be inaccessible to the silencing machinery" (see page 299, column1 paragraph 2). Lecellier et al. further state that "...the most critical point in the development of RNAi-based therapeutics concerns the delivery of effector molecules" (see page 299, paragraph 1). Haasnoot et al. (J Biomed Sci 2003: 10, pages 607-616) recognizes the same issues and states the "major problem for using RNAi as a tool to inhibit viral replication is the fact that it is still difficult to predict the effectiveness of a certain siRNA....In addition, viral escape from RNA silencing is clearly a problem for developing effective RNAi-based antiviral therapy" (see page 614, column 1 last paragraph and column 2 first paragraph).

Calvez et al. (Viral Journal 2004, 1:1-6) notes that prevention and treatment of viral infections involves two aspects such as preventing viral entry into host cells and inhibiting viral amplification by targeting the viral mRNA with inhibitors such as siRNA and states "Some major technical hurdles need to be overcome before siRNA-based

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anti-viral prophylaxis and treatment move into the clinics. Especially, intracellular delivery of siRNA needs to be greatly improved..." (see pages 1 and 5).

Moreover, even Applicants recognize the hurdles siRNA based anti-viral therapeutics face before clinical use as a preventative method for influenza viral infection becomes a reality. Ge et al. (Virus Research 2004, Vol. 102: 37-42) acknowledge that RNAi appears to be ideal for inhibiting influenza virus infection (see page 39), but notes that "an effective siRNA-mediated prevention and treatment of influenza virus infection requires efficient non-toxic means to deliver siRNAs..." before such siRNAs become a clinical reality for prevention of viral diseases (see page 40).

As outlined above, it is well known that there is a high level of unpredictability in the siRNA art for therapeutic *in vivo* applications for prevention of viral infections, namely influenza virus. The scope of the claims in view of the specification as filed together do not reconcile the unpredictability in the art to enable one of skill in the art to make and/or use the claimed invention.

Given the teachings of the specification as discussed above, one skilled in the art would not know *a priori* whether introduction of siRNA compounds *in vivo* by the broadly disclosed methodologies of the instantly claimed invention, would result in successful prevention of influenza virus or any transcript associated with influenza virus. Without further guidance, one of skill in the art would have to practice a substantial amount of trial and error experimentation, an amount considered undue and not routine, to practice the instantly claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 38-42, 49, 81-90 and 98-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal et al. (US Patent No. 5,194,428), Tuschl et al. (WO 02/44321), Gautum et al. (Molecular Therapy 2000, Vol. 2(1); 63-70) and Kircheis et al. (Gene Therapy 1997: 4: 409-418).

The claims are drawn to methods of inhibiting a transcript associated with a influenza virus, or methods of treating or preventing or treating an influenza virus or a clinical condition associated with overexpression or inappropriate expression of an influenza transcript, comprising administering an siRNA in combination with a cationic polymer, wherein said administration may be intravenous or intranasal, or is inhaled, or is delivered by aerosol, or wherein said inhibition is in the lung, or not in the lung, or wherein said combination is delivered with a delivery enhancing agent which may be an antibody or fragment or ligand.

Agrawal et al. teach targeting an antisense compound to a gene encoding an influenza virus and inhibiting expression of viral PB1 from said gene (see column 5, lines 5-25). Agrawal et al. teach said antisense compound has at least 8-20 nucleotides that are complementary to the target region and teach administration of the antisense compound intravenously or orally (see column 9). Agrawal et al. does not teach the

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using a siRNA targeted to a viral PB1 or teach using a siRNA and a cationic polymer and further do not teach using an antibody or ligand to specifically target a cell.

Tuschl et al. teach the use of siRNA compounds to inhibit gene expression.

Tuschl et al. teach siRNA are the new alternative to antisense compounds and have improved efficacy and safety (see page 3). Tuschl et al. teach a method of using siRNA to infect cells and teach modulating of the function of a target gene, such as a viral target gene (see page 8). Tuschl et al. teach the siRNA can be delivered using a carrier system (see page 8) and teach the siRNA can be administered by injection or intranasally. Additionally, Tuschl et al. teach a vector capable of expression of a siRNA (see page 7).

Gautam et al. teach a method of efficiently delivering nucleic acids along with a cationic polymer, polyethyleneimine (PEI), into the lungs of a mouse (see Figure 1).

Gautam et al. teach the nucleic acid-PEI complex was delivered via aerosolization (see page 64).

Kircheis et al. teach coupling a transferrin or an anti-CD3 antibody to a PEI-nucleic acid complex for targeted delivery of the complex to a particular cell.

It would have been obvious to one of skill in the art to substitute a siRNA molecule for the antisense molecule in the method of inhibiting viral PB1 gene taught by Agrawal et al. It would have further been obvious to use the cationic polymer PEI to efficiently deliver the siRNA to the cell of interest and further obvious to incorporate a ligand or antibody to the PEI-siRNA complex for targeted delivery to a specific cell type.

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One of skill in the art would have been motivated to use a siRNA instead of an antisense compound because Tuschl et al. teach silencing of gene expression is more efficient and sequence specific than with using an antisense compound. Further one of skill in the art would have been motivated to deliver the siRNA using a delivery agent such as PEI given Gautam et al. teach PEI can efficiently deliver a nucleic acid to cells and also teach PEI can protect the nucleic acid from degradation. Further, because Gautum et al. teach PEI can be aerosolized along with nucleic acid and delivered to lung tissue, one of skill in the art would have been motivated to use PEI as a delivery agent in a method of treating Influenza virus which affects lung cells. Kircheis et al. teach coupling of cell binding ligands to PEI for targeted gene delivery and one of skill in the art would have been motivated to couple a specific ligand or antibody to the PEI-siRNA complex to enhance the target specific delivery to lung cells. Ensuring the siRNA is delivered specifically to the cell of interest would increase the siRNAs capability of mediating RNAi and one of skill in the art would have been motivated to use a ligand or antibody coupled to the PEI-siRNA complex.

There would have been a reasonable expectation of success at using a PEI for delivery of a siRNA into cells, particularly lung cells given Gautum et al. teach delivery of a nucleic acid using PEI. One would have expected siRNA to be capable of delivery using a cationic polymer such as PEI given siRNA is a nucleic acid and should be delivered similarly. One would have expected to be able to conjugate any ligand or antibody onto a PEI-siRNA complex given Kircheis et al. teach how to conjugate a

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ligand or antibody onto a PEI-nucleic acid molecule and teach efficient cell targeting properties.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicant's Arguments

Re: Claim Rejections - 35 USC § 112

The rejection of claims 38-42, 49, 84-90 and 99 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the new grounds of rejection above necessitated by claim amendments filed .

Response to Applicants Arguments

Re: Claim Rejections - 35 USC § 102

The rejection of claims 38-42, 49, 81-90, 98 and 99 under 35 U.S.C. 102(e) as being clearly anticipated by Beigelman et al. (US Pre-Grant Pub Number 2003/0148928 A1) is maintained for the reasons of record.

Applicants arguments filed 12/04/2006 are acknowledged but are not found persuasive. Applicant argues Beigelman does not describe cationic polymers but instead describes cationic lipids and the lipids described by Beigelman are not polymers. Applicant further argues the instant specification defines lipid as an entity that is different from a polymer argues that because the description of polymers falls on a different page than lipids, the instantly claimed polymers are not lipids. This line of

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reasoning is not convincing. There is not a limiting definition of polymer in the instant specification and further Applicant does in fact submit that a polymer can be a lipid consisting of multiple lipid monomers (see remarks page 9) and as stated in the Advisory Action mailed 01/29/2007, a lipid is a long chain of carbon monomers and therefore would meet the limitations of the instant claims.

Applicant further argues that the delivery molecules taught Beigelman et al. require them to be conjugated to a nucleic acid and the instant claims specify that the RNAi inducing entity is not a conjugate. This argument is not convincing because the claims are drawn to a delivery composition comprising an RNAi-inducing entity and a delivery agent and does not recite or is not limited to the entity and delivery agent as not being a conjugate. Applicant points to new claim 100 as specifically limiting the instant invention by the use of "consisting of". This is not convincing because the claims are still drawn to a delivery composition *comprising* an RNAi-inducing entity and a delivery agent and does not recite this composition is not a conjugate.

Thus, the rejection of record is maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight

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/Kimberly Chong/
Examiner
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